Remarks

This Amendment is responsive to the Office Action mailed February 27, 2007, which sets a three-month shortened statutory period for response, to end May 27, 2007. With this Amendment, Applicants cancel claims 5 and 13-15, and amend claims 1 and 2, leaving claims 1-4, 6-12, and 16-19 pending and under consideration.

Claim Rejections – 35 U.S.C. § 112, First Paragraph

The Office Action rejects claims 1-19 under 35 U.S.C. § 112, first paragraph, as allegedly failing to satisfy the enablement requirement. The Action indicates that although the specification enables the use of "certain soluble ingredients from a microorganism as an adjuvant, [it] does not reasonably provide enablement for the use of *any* soluble ingredient of a microorganism." (Emphasis added.) Applicants assume that by "any" the Examiner means "every."

In response, Applicants respectfully submit that the claims are in fact enabled by the specification. In particular, Applicants respectfully note that the specification clearly conveys how to obtain the soluble ingredient by washing with an organic solvent and/or hot water. Applicants note that the claims do not require any characterization of the soluble ingredient, or any further fractionation. The specification clearly conveys how to make the claimed immunoadjuvant.

It appears that, on some level, the Office may believe that not all soluble fractions derived from a cell or tissue will result in immunomodulatory activity. However, Applicants note that the claims do not require that each element of the recited soluble

fraction exhibit an immunomodulatory activity. All that the claims require is the formation of an immunoadjuvant prepared according to the claimed steps.

Moreover, to the extent that the Office's position is based upon an assertion that the recited soluble fraction, when combined with solidified material, will not *result* in an immunoadjuvant, the Office Action fails to support its position. The Examiner cites Barot-Ciorbaru et al. for the argument that only certain soluble extracts possess immunomodulatory activity. However, the Action fails to show that a "soluble ingredient . . . removed by washing with an organic solvent and/or hot water" would necessarily *not* result in an immunoadjuvant.

In view of the foregoing remarks, and the amendment to claim 1, Applicants respectfully request withdrawal of the rejection.

Claim Rejections – 35 U.S.C. § 103

The Office Action rejects claims 1-19 under 35 U.S.C. § 103(a) as allegedly unpatentable over Ohno et al. (CA 2362578) and Ravindernath et al. (U.S. Patent No. 6,218,166).

Applicants initially note that the present invention was made on the basis of the finding that a fragment as recited in claim 1, i.e., a solidified biological material, had desirable properties as an adjuvant carrier for immobilizing a soluble ingredient derived from a microorganism. In the field of tumor immunology, a desired adjuvant carrier would not exhibit the undesirable activity in the solid state and biodegradable form, as discussed in the Background section of the specification. Thus, there was a need in the

art for an invention such as the presently claimed invention, and the presently claimed invention solved those prior problems.

Turning to the cited art, Applicants respectfully note that Ohno et al. (CA 2,362,578) teaches tumor vaccines containing particles prepared from solidified tumor material and at least one cytokine and/or cytokine inducer. (See Abstract of Ohno et al.) The tumor vaccines may optionally include an adjuvant, but such is not required. (Abstract.) As the Office Action recognizes, Ohno et al. does not teach or suggest that a solidified tumor material can be immobilized to the optional adjuvant, or that there is any desirability of such immobilization.

The Office Action cites Ravindernath et al. (U.S. Patent No. 6,218,166) for its teaching of immobilization of a bacteria-derived soluble adjuvant, monophosphoryl lipid, to an intact cell. The Office Action asserts that a person of skill in the art would have been motivated to immobilize a bacterial adjuvant taught by Ravindernath et al. to the formalin-fixed tissue taught by Ohno et al.

In response, Applicants respectfully note that Ravindernath et al. does not suggest a use for an adjuvant alone, i.e., without being attached to a "whole cell." Thus, to suggest that one of skill in the art would "immobilize a bacterial adjuvant taught by Ravindernath et al." without a whole cell affixed thereto – to anything – is to ignore the totality of the disclosure of Ravindernath et al. Moreover, a person of skill in the art would not replace the whole cell of Ravindernath et al. with a formalin fixed (or any otherwise solidified) cell from Ohno et al. with any expectation of success.

Ravindernath et al. emphasizes the importance of the use of whole cells:

> The use of *whole cells* is an important feature of the invention that imparts many particular advantages. For example, tumor-associated antigens

> (TAAs) no longer have to be first identified or purified. omitting the purification step is a marked improvement in terms of time, difficulty and costs and, even more importantly, ensures that the antigens are presented in their natural environment. Isolation of TAAs has previously involved harsh conditions, such as extraction in 3 M KCl, which may destroy or modify certain of the epitopes. However, any extraction method that removes the TAA from the membrane environment is likely to alter its immunogenic properties, and it is an advantage of the present invention that this is no longer necessary.

(Column 4, lines 12-26; emphasis added.)

Ravindernath et al. further emphasizes, in its general description of the method for making its complex, why living cells must be used.

> The present invention provides a simple, but surprisingly effective method of preparing an adjuvant-incorporated cell complex, which method comprises incubating cells in an adjuvant-suspended culture media at an appropriate temperature and for a sufficient period of time, for example, as described herein in Example 5 and Example 8.
>
> . . .
>
> The cell surface-associated adjuvants may be conjugated to any available membrane component, as exemplified by proteins, glycolipids and phospholipids in the membrane bilayer. Data is presented herein to show that the adjuvant-incorporated cells of the invention have adjuvants incorporated into the bilayer, and are not simply cells coated with, or loosely associated with, adjuvants. The adjuvant-incorporated cells of the invention are associated with effective amounts of adjuvants and yet the integrity of the cell is maintained.

(Column 4, line 56 – column 5, line 10.)

As it is clear that Ravindernath et al. complexes its adjuvants to its whole cells by incubating a living cell culture in an adjuvant-containing media, there would be no expectation of success in replacing Ravindernath et al.'s whole cells with Ohno et al.'s formalin-fixed cells. Formalin-fixed cells are no longer capable of living in cell culture media, and thus, there would be no expectation of success in this replacement.

In view of the foregoing remarks, Applicants respectfully submit that the Office has failed to establish a *prima facie* case of obviousness and respectfully request withdrawal of the obviousness rejection.

Obviousness-Type Double Patenting Rejection

The Office Action rejects claims 1-5, 7, and 9-19 for obviousness-type double patenting over claims 1, 3, 6, 7, and 17-19 of copending U.S. Application No. 09/890,266. The Action asserts that while the claims are not identical, they are not patentably distinct.

Initially, Applicants note for the Examiner that the '266 application has now been allowed and issued as U.S. Patent No. 7,247,310.

With regard to the rejection, Applicants respectfully note that the present claims are directed to an immunoadjuvant including a soluble component immobilized to solidified tissue, whereas claim 1 of the '266 application is directed to a vaccine comprising solidified tumor tissue or cells and at least one cytokine. Only claim 7 of the '266 application even refers to an adjuvant. Regardless, none of these claims, even in view of the specification of the '266 patent application, suggests an immunoadjuvant including a soluble component immobilized to solidified tissue.

In view of the foregoing, Applicants respectfully submit that a case of obviousness-type double patenting does not exist in this instance and that the present claims are patentably distinct from the claims in the '266 application, and Applicants respectfully request withdrawal of the rejection.

Conclusion

In view of the foregoing remarks and amendments, Applicants respectfully submit that all pending claims are allowable over the art of record and in condition for allowance. If there should be any questions, the Examiner is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted,
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August 21, 2007
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